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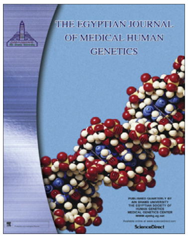

ORIGINAL ARTICLE

Heritability of fear: Ukrainian experience

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Abstract *Background:* A wide range of normal and clinically significant behavior traits, including fears, were intensively studied and heritability coefficients were obtained for many of them. A heritability value is a population-based trait, so it may significantly vary in different human populations. In the former Soviet Union, research on human behavior traits was mostly tabooed. Ukraine is a population with a unique history and cultural background and with a specific multi-ethnic composition. Until 1991, Ukraine was part of the former Soviet Union. The current research is devoted to heritability of fear assessment in Ukrainian megapolice sample.

Subjects and methods: 2305 individuals (741 males and 1564 females), aged 14–72 years, participated in the current study. Data were collected during 2004–2007. All participants lived in Ukraine and were Slavs (predominantly Ukrainians and Russians). Most of them were Kharkov city residents (Kharkov is the second city in Ukraine by its population size after the capital Kiev city, and Kharkov region includes about 1,730,000 inhabitants). Most participants were engaged without relatives and were used only for population distribution evaluation. Some volunteers were enrolled with a relative of the first degree of relatedness (with a parent or a sibling). These formed 352 parent–offspring pairs and 104 sibling pairs. Spouses were enrolled in the experiment for a potential assortative mating effect searching. The total number of marital couples was 74.

24 emotional states of fear have been studied by Ivleva–Shcherbatyh questionnaire, which was developed and validated by Russian psychologists in Slavs samples.

Evaluation and decomposition of total phenotypic variance were performed according to the classical Falconer approach, based on correlation coefficients between relatives. Assortative mating effect was taken into account and correlation coefficients between relatives were adjusted for traits with statistically significant correlation coefficients between wives and husbands.

Results: As a result of the research, correlation coefficients of fears ρ between relatives and mates were obtained in the range 0.18–0.77. In majority of cases, correlation coefficients were higher in sibling pairs compared to «parent–offspring» pairs. For three fears (psychiatric disorders development, disease of relatives, and suicide commitment) there was a positive assortative mating in the population (correlation coefficients ρ were in the range 0.35–0.43), so for these traits, correlation

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coefficients' modification between relatives was needed to be done. Heritability coefficients of nine types of fear were in the range 26–48%, among them the lowest heritability coefficient was recorded for fear of suicide commitment and the highest one was recorded for fear of aggressive behavior possibility to the relatives.

Conclusions: The conducted research demonstrated genetic component presence for nine types of fear – psychic disorder development, complications in personal life, making responsible decisions, senility, closed spaces, sexual dysfunction, suicide commission, speaking in public, and aggressive behavior possibility to relatives. It helps to consider these fear perspectives for further molecular-genetic analysis in Ukraine.

1. Introduction

The final aim of genetic analysis for any trait is searching for genes, which are responsible for its formation, their localization in a genome, and possible variant. Further analysis targets how products of these genes influence metabolic pathways, leading to trait formation. Many human and other biological species can be traced this way. Generally, it is clear for relatively simple traits, such as blood groups, single-gene diseases, etc. More complicated situation is with the so named, 'quantitative traits', which are associated with many traits of behavior. Nevertheless, such analysis is possible, and its algorithm on the first stage suggests a phenotype inventory, forming heritability estimation. The phenotype inventory means an assessment of trait variability in a population.

Both environmental factors and genes influence human behavior traits. Another thing which should be taken into consideration and can attribute to phenotypes is complex interactions between genes and environment. People in a population vary in the genotypes for behavior traits. The genotypic part is due to a combined effect of all loci, including possible allelic interactions within loci (dominance) and between loci (epistasis). Heritability is the proportion of phenotypic variation (V_P) that is due to variation in genetic values (V_G). Broad-sense heritability can be calculated as $h^2 = V_G/V_P$ and demonstrates the proportion of phenotypic variation due to genetic values that may include effects due to dominance and epistasis. Narrow-sense heritability can be calculated as $h^2 = V_A/V_P$ and shows only that proportion of genetic variation that is due to additive genetic values (V_A). The value of heritability always lies between 0 and 1 (or between 0% and 100%) [1].

After heritability assessment, further analysis is conducted due to the heritability value. If a heritability coefficient is close to zero, we can make a conclusion that inter-individual differences are caused by different environmental conditions. On the contrary, if h^2 is close to one, a quite opposite conclusion can be made (inter-individual differences are mostly due to genetic differences). Proof of a genetic influence makes a sense for a further gene search. Without prior population analysis and heritability estimation, the search of these genes is ineffective [2].

A wide range of normal and clinically significant behavior traits were intensively studied and heritability coefficients were obtained for many of them, such as mental ability [3,4], altruism and aggression [5,6], suicidal behavior [7,8], borderline personality disorder [9], fears [10–12] etc.

The trait which is often under study in genetic investigations is fear. In some cases, the intensity of fear can go beyond a normal range (often in the strengthening side). Strong intensity of fear to a stimulus of inadequate strength is a component of mental disorders, particularly, panic attacks, phobias, and obsessive–compulsive syndrome. The prevalence of such disorders in the world population is relatively high [13], weakening people's health and quality of life [14].

Nonetheless, in spite of many studies done on fear, many questions are not yet clarified. Moreover, a heritability value is a population-based trait, so it may significantly vary in different human populations. In the former Soviet Union, research on human behavior traits was mostly tabooed. Ukraine is a population with a unique history and cultural background and with a specific multiethnic composition [15–18]. Until 1991, Ukraine was part of the former Soviet Union. The current research will fill some gaps on the "behavioral map" of Ukraine in relationship with fear heritability estimation.

2. Subjects and methods

2.1. Subjects

2305 individuals (741 males and 1564 females), aged 14–72 years, participated in the current study. Data were collected during 2004–2007. All participants lived in Ukraine and were Slavs (predominantly Ukrainians and Russians). Most of them were Kharkov city residents (Kharkov is the second city in Ukraine by its population size after the capital Kiev city, and Kharkov region includes about 1,730,000 inhabitants).

The volunteers were enrolled randomly in different schools, colleges, and universities of Kharkov city and Kharkov region. They were school children of 10th and 11th classes (schools of Kharkov city Nos. 22, 23, 24, 27, 56, 91, 95, 148 and 156, and the Pesochin Collegium of Kharkov region) or college (Kharkov Building Secondary Technical School) and university (V.N. Karazin Kharkiv National University, National University of Pharmacy, National Technical University "Kharkov Polytechnic Institute" and Kharkov National Medical University) students of different courses (1st–5th), so the age of this subgroup of participants varied from 14 to 23.

Most participants were engaged without relatives and were used only for population distribution evaluation. Some volunteers were enrolled with a relative of the first degree of relatedness (with a parent or a sibling). These formed 352 parent–offspring pairs and 104 sibling pairs.

Spouses were enrolled in the experiment for a potential assortative mating effect searching. The total number of marital couples was 74.

Data collection was made taking into consideration ethical requirements and Helsinki guidelines for human volunteers' participation in scientific studies (*World Medical Association Declaration of Helsinki, Ethical Principles for Medical Research Involving Human Subjects*). All participants gave their written consent and received the interpretation of their results as a reward for an experiment inclusion.

2.2. Psychological tools

24 emotional states of fear have been studied by Ivleva–Shcherbatyh questionnaire, which was developed and validated by Russian psychologists in Slavs samples [19]. The examined fear sources were as follows: animals, darkness, psychic disorders development, disease of relatives, street attack, communication with authorities, complications in personal life, making responsible decisions, old age, pain, poverty, uncertainty about future, exam, war, death, closed space, height, depth, adverse changes in the case of relatives' disease, the possibility of disease, sexual dysfunction, suicide, speaking in public, the possibility of aggressive behavior with relatives. Each fear was estimated on a point scale, ranging from 1 to 10.

2.3. Heritability estimation

Evaluation and decomposition of total phenotypic variance were performed according to the classical Falconer approach [2], based on correlation coefficients between relatives. Correlation coefficients were calculated for parent–offspring pairs, siblings and spouses. Statistical significance was accepted on the level $p \leqslant 0.05$ [20]. Because previous distribution checking has shown no compliance with a Gaussian law, non-parametric (Spearman) correlation coefficient ρ was used for parent–offspring pairs (ρ_p, mother–daughter, father–daughter, mother–son, and father–son), sibling pairs (ρ_s male and female sibling pairs, brother–sister) and spouses (ρ_{hw}). Assortative mating effect was taken into account, and correlation coefficients between relatives were adjusted for traits with statistically significant correlation coefficients between wives and husbands (ρ_{hw} by means of formula, $\rho' = \frac{\rho}{1+\rho_{hw}}$, where ρ' stands for modified correlation coefficient). Modified correlation coefficients between relatives were used for component decomposition of total phenotypic variance by means of formulas, $G_a = 2\rho_p$; $G_d = 4(\rho_s – \rho_p)$; $G = G_a + G_d$; $\mathrm{E} = 1–G$, where G is total genetic component, G_a is its additive, and G_d is its dominant components, E means environmental component.

Database was formed in Microsoft Excel program. The calculations have been made by Statistics 6.0 software program.

3. Results and discussion

Traditional approach in heritability estimation is based on correlation analysis among relatives pairing. Genetic component extraction from received correlation coefficients is the most complicated. If the trait completely depends only on a genotype, a correlation coefficient between relatives will be equal to kinship coefficient. But often a correlation coefficient is higher than kinship coefficient. There are at least two reasons why correlation coefficients between relatives are so high. One of them is positive assortative mating on trait under study. Parents' phenotypic similarity on a specific trait increases the correlation coefficients in offspring comparatively to its expected value (if marriages are formed randomly). The other reason for increased correlation coefficient between relatives is an influence of shared family environment. Relatives, as a rule, have similar socio-economic position, equal access to education and similar upbringing. All this promotes trait development in one direction, and increases similarity. That is why it is more correct to examine relatives of different relationship degrees, who live separately although in such situation, relatives can create a common environment according to their own genotypes and their genes are realized in this environment. According to geneticists' opinion, it is the main reason, which does not give the opportunity to separate completely the genetic and environmental influences on traits [2]. In some countries, where the history of behavior genetics comes back to a past century, registers of twins and adoptees were generated and maintained. There is also a possibility to conduct a monitoring of certain contingent and make conclusions about trait variability. This infrastructure is totally absent in Ukraine. Low genealogical culture of modern population strongly interferes with conductance of such research. That is why there is a possibility only to perform correlation analysis in two categories of relatives (“parent–offspring” and “sibling–sibling”). Relative pairs are initially analyzed separately to avoid a sex effect. The necessity of a separate correlation analysis conductance even among relatives with the same degree of kinship (mother–daughter, father–daughter, one- and heterosexual sibling, etc.) follows from general genetic ideas about the possibility of different traits' transmission, depending on sex of a parent and a child. It is more obvious for X- and Y-linked inheritance, as well as for complex polygenic traits for which there is a principal gene, located in the sex chromosomes. Preliminary analysis in narrower groups is also desirable for traits, displaying sex dimorphism. However, in practice and in such cases, the calculations of the average population correlation coefficients between relatives of different categories are used, they are based on the previously calculated correlation coefficients in narrower groups, so as the heritability coefficient, which is a general population characteristic. The probability of a particular pair formation in the population is taken into consideration [21].

There are more unisexual female pairs and less – unisexual male pairs in the current research among “parent–offspring” and “sibling” pairs. Numerically, unequal related pair presentation of different categories is an ordinary problem of many population researches, which enroll people on a free base (without payment for participation). It is due to male and female inequality in wishing to take part in a study (females are more cooperative). In accordance with this approach, weighted mean correlation coefficients have been used in this investigation.

Correlation coefficients in groups, “parent–offspring” and “siblings” according to 24 different fears are shown in Table 1. Significant correlation coefficients have been detected for 12 types of fear in parent–offspring pairs and four statistically significant types of fear were found for siblings. Just these last four types of fear have the biggest values of correlation

Table 1 Correlation coefficients (ρ) on fears in pairs «parent–offspring» and in sibling pairs.

Fears	Relatives				
	Mother–daughter (n = 81)	Father–daughter (n = 34)	Mother–son (n = 14)	Father–son (n = 11)	Mean weighted (n = 140)
Animals	0.12	0.17	−0.45	0.18	0.08
Darkness	0.14	0.18	−0.13	0.24	0.14
Mental disorder development	0.24*	0.12	−0.19	0.77**	0.21*
Diseases of relatives	0.20	0.21	0.23	0.75**	0.24**
Street violence	0.21	0.00	−0.41	0.46	0.13
Communication with an authority	0.14	0.18	−0.24	0.15	0.12
Problems in a private life	0.19	0.22	−0.33	0.52	0.19*
Responsible decision making	0.24*	0.03	0.27	−0.04	0.18*
Aging	0.21	0.22	−0.16	0.41	0.18*
Pain	0.28**	−0.23	−0.28	0.76**	0.15
Poverty	0.23*	0.08	−0.07	0.54	0.21*
Future uncertainty	0.01	−0.24	−0.14	0.54	−0.03
Exam	0.18	−0.09	0.30	0.27	0.09
War	−0.05	0.21	0.20	0.68*	0.14
Death	0.39***	−0.09	0.28	0.57	0.24**
Confined spaces	0.25*	0.23	−0.22	0.10	0.21*
Height	0.24*	0.02	−0.44	0.14	0.14
Depth	0.08	0.26	−0.36	0.55	0.14
Problems in the case of diseases of relatives	−0.09	0.11	−0.17	−0.16	−0.06
Disease possibility	0.36**	−0.22	−0.12	0.45	0.15
Sex function disorders	0.33**	0.06	0.29	0.00	0.24**
Suicide commitment	0.09	0.32	0.25	0.24	0.18*
Public speech	0.13	0.28	0.32	0.54	0.19*
Aggression possibility to relatives	0.17	0.18	0.39	0.31	0.23**

Fears	Relatives			
	Male siblings (n = 2)	Female siblings (n = 10)	Brother–sister (n = 16)	Mean weighted (n = 28)
Animals	–	0.43	−0.45	−0.04
Darkness	–	0.26	0.27	0.20
Mental disorder development	–	0.33	0.15	0.27
Diseases of relatives	–	0.31	0.38	0.48**
Street violence	–	0.27	−0.50*	−0.07
Communication with an authority	–	0.62*	0.32	0.35
Problems in a private life	–	−0.19	0.44	0.24
Responsible decision making	–	0.10	−0.30	−0.13
Aging	–	0.39	0.18	0.24
Pain	–	−0.15	0.38	0.16
Poverty	–	0.25	0.66**	0.47**
Future uncertainty	–	0.30	0.28	0.28
Exam	–	−0.21	0.44	0.22
War	–	0.37	−0.12	0.17
Death	–	0.51	0.29	0.38*
Confined spaces	–	−0.13	0.37	0.23
Height	–	0.58	0.45	0.47**
Depth	–	0.57	0.29	0.22
Problems in the case of diseases of relatives	–	0.22	0.12	0.26
Disease possibility	–	0.13	0.28	0.21
Sex function disorders	–	0.43	0.21	0.28
Suicide commitment	–	0.03	0.14	0.12
Public speech	–	0.17	0.34	0.27
Aggression possibility to relatives	–	0.63*	−0.16	0.30

Notes: n – number of participants, ρ – Spearman correlation coefficients.

coefficients: relative's disease – $\rho = 0.48$ ($p < 0.01$), poverty – $\rho = 0.47$ ($p < 0.01$), death – $\rho = 0.38$ ($p < 0.05$), height – $\rho = 0.47$ ($p < 0.01$).

Most investigations meet the fact that marriages are formed not randomly on behavioral, somatic and social features [22]. Thus, moderate positive correlation between spouses is found

Table 2 Statistically significant correlation coefficients between spouses on some fears.

Fears	*n*	ρ
Mental disorder development	38	0.41^{**}
Diseases of relatives		0.35^{*}
Suicide commitment		0.43^{**}

Notes: n – number of participants, ρ – Spearman correlation coefficients.

for anthropometric characteristics ($r = 0.10$–0.30) and IQ ($r = 0.37$), and it is larger for physical attractiveness ($r = 0.38$–0.52) and educational level ($r = 0.46$). On personal characteristics, the similarity of partners is lower ($r = 0.23$–0.47, in average $r = 0.15$), while on personal values it is rather higher ($r = 0.20$–0.58). The highest correlation between the partners is observed for traits such as religiosity, conservatism, and authoritarianism ($r = 0.40$–0.70). Correlation for traits manifestation is also observed in accordance with age at the moment of marriage [23].

Positive correlation between partners of any reason is a prerequisite of assortative mating, related to deviation from panmixia state. Effects of positive assortative mating are similar to inbreeding effects. Positive correlation between the partners leads to increased correlation coefficients between relatives. Therefore, correlation between the spouses is necessary to use for modifying (adjustment) correlation coefficients between relatives during genetic analysis. With a positive assortative mating, the probability of marriage formation for similar partners' phenotypes is higher than in the case of statistical random situation. Under the assumption that the phenotype is a direct or indirect reflection of a genotype, positive assortative mating leads to the fact that the genotype frequencies change from generation to generation; and there are less heterozygotes and more homozygotes. Though, the consequences of positive marital assortativity are similar to inbreeding effects in the change of genotype frequencies, increasing homozygotes portion, there are significant differences between these two phenomena. Thus, under inbreeding, the selection of a marital partner is based on kinship; as a result, inbreeding affects all gene loci. Positive assortative mating influences only genotype frequencies, which are involved in specific phenotypic traits displayed.

At negative assortative mating, partners are selected by phenotype dissimilarity. As a result of negative assortative mating, there are more heterozygotes in a population with each generation. Negative assortative mating promotes genetic subdivision smoothing between groups and quickly destroys genetic differences between historical subpopulations, which unite and practice marital structure building on the base of negative assortative mating.

Results of correlation analysis on fears in marital couples (statistically significant correlation coefficients) are shown in Table 2. Table 3 presents modified correlation coefficients in pairs of relatives according to all types of fear, for which significant correlation coefficients in marital couples have been detected. As one can see, the presence of positive relationship between the partners may artificially increase correlation coefficients in relatives to one and half times.

Table 3 Results of correlation analysis (modified correlation coefficients) in relative pairs adjusted to positive assortative mating effect.

Fears	Parent–offspring pairs	Sibling pairs
	Modified correlation coefficients ρ	
Mental disorder development	0.15^{*}	
Diseases of relatives	0.18^{*}	0.36^{*}
Suicide commitment	0.13^{*}	

Notes: n – number of participants, ρ – Spearman correlation coefficients.

Table 4 Results of component phenotypic variance decomposition.

Fears	G_A, %	G_D, %	G_{tot}, %	E, %
Mental disorders development	30		30	70
Diseases of relatives	36	72	*108*	
Problems in a private life	38		38	62
Responsible decision making	36		36	64
Ageing	36		36	64
Poverty	42	*100*	*100*	0
Death	48	56	*100*	0
Confined spaces	42		42	58
Height		*100*	*100*	0
Sex function disorders	48		48	52
Suicide commitment	26		26	74
Public speech	38		38	62
Aggression possibility to relatives	46		46	54

Notes: G_{tot} – total genetic component, G and G_D – additive and dominant components of total genetic component, E – environmental component. Values in italic have no arithmetic sense but are limited by 100%.

Heritability assessment of fear has been conducted after correlation analysis in the pairs of relatives, taking into account the assortative mating. For some fears during conduction of component analysis, it became possible to share additive and dominant components from total genetic component, and obtained heritability coefficients reflected heritability “in broad sense.” For some fears heritability has been determined only “in narrow sense”. This was true for such fears, according to which a positive statistically significant correlation coefficient was observed only in pairs of “parent–offspring”. Traits have been found, for which positive significant correlation coefficient has been detected only in sibling pairs, but in “parent–offspring” pairs it was not statistically significant and close to zero.

Fear without statistically significant correlation coefficients set a particular group. However, even in this case, the conclusion about the absence of genetic influence on these traits cannot be absolute. The fact is that the geneticists involved in the study of heritability of complex behavioral traits, faced a similar problem in the 1990s. Scientists found a group of so-called emergent traits, which during the study of certain categories of relatives (parent–offspring, siblings) did not display any common family effect. However, during monozygotic twins study on the same traits, the significant similarity of traits of partners, bringing up either together or separately, was found [24].

The current research about fear, by which the heritability assessment of quantitative behavioral traits in classical way became impossible to perform, can also be emergent. To prove this, analysis of monozygotic twins is necessary. Besides, it is possible that these heritability traits are close to zero. Fear, for which the heritability assessment by classical method was feasible, provisionally can be attributed to traits with moderate heritability. Obtained values of heritability can possibly be maximum, as far as common family environmental factors are present in the correlation coefficients between relatives; it is impossible to isolate them yet. We can get more accurate results, having information about relatives of the same generation, living separately (cousins, half-cousins, half-siblings etc.). Heritability coefficients for all types of fear, for which significant correlation coefficients were detected, are shown in Table 4.

The obtained heritability coefficient values in the present research cannot be considered absolute for the whole population, as the possibility of different heritability values in other age groups are not excluded. For example, the results of the longitudinal twin investigation in Sweden have shown the ontogenetically dynamic theory consistency of genetic conditionality of different types of fear as opposed to ontogenetically stable theory. Ontogenetically dynamic theory suggests that at different stages of individual development (ontogenesis), different genes of predisposition to fear and phobias are activated. In this investigation, including analysis of 2490 twins, their parents (for younger children) and the examined (since the age of 13) studied three types of fear – situational fears, fear of animals and fear of blood/injuries. Particularly, it was shown that the heritability of situational fear in the mentioned age range made up 50%, 68%, 69% and 59%. As to other two types of fear, the tendencies were similar. Scientists suggest that different heritability fears in different life periods form during the process of evolution, as far as a change in ranking of potential danger sources happens in children with age. Strong fear in a child may weaken in a teenager, and conversely, unknown fears in early childhood may be realized only over time [25].

4. Conclusions

The conducted research demonstrated genetic component presence for nine types of fear – psychic disorder development, complications in personal life, making responsible decisions, senility, closed spaces, sexual dysfunction, suicide commission, speaking in public, and aggressive behavior possibility to relatives. It helps to consider these fear perspectives for further molecular-genetic analysis in Ukraine.

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